J. Chil. Chem. Soc., 58, Nº 4 (2013)

SYNTHESIS, THERMAL BEHAVIOR, AND AGGREGATION IN AQUEOUS SOLUTION OF POLY(METHYL METHACRYLATE)-B-POLY(2-HYDROXYETHYL METHACRYLATE)

B. ACEVEDO[1], F. MARTINEZ[2], A. F. OLEA[1]*

[1]*Departamento de Ciencias Químicas, Facultad de Ciencias Exactas, Universidad Andrés Bello, Quillota 980, Viña del Mar, Chile.*
[2]*Departamento de Ciencias de los Materiales, Facultad de Ciencias Físicas y Matemáticas, Universidad de Chile, Santiago, Chile*
(Received: July 29, 2013 - Accepted: August 28, 2013)

ABSTRACT

Amphiphilic block copolymers of poly(methyl methacrylate) PMMA and poly(2-hidroxyethyl methacrylate) PHEMA were synthesized by a two–step atom transfer radical polymerization (ATRP). Copolymers with various degrees of polymerization and different relative block sizes were obtained. The structure of the resulting polymers have been characterized and verified by FT–IR and ^{1}H–NMR, molecular weight were determined by size exclusion chromatography analyses. The thermal properties of these polymers were investigated by differential scanning calorimetry DSC and thermogravimetric analysis TGA. The glass transition temperature of mono halogenated PMMA increases from 116 ºC to 123 ºC with increasing molecular weight, whereas the glass transition temperature of block copolymers depends slightly on polymer structure. The derivatives of TGA curves indicate that thermal degradation occurs in one stage. The self-assembly of PMMA-b-PHEMA in aqueous solution have been investigated by fluorescence probing methods. The critical micelle concentrations are in the range 10^{-6} – 10^{-7} M. The micropolarity sensed by pyrene is higher than in aggregates formed by block copolymers based on polystyrene.

Keywords: Block copolymers, glass transition temperature, thermogravimetric analysis, critical micelle concentration, fluorescence probing methods.

1. INTRODUCTION

Over the last decades much attention has been devoted to amphiphilic block copolymers because of their potential applications in drug delivery[1-6], imaging, catalysis, etc. One of the main properties of these copolymers is the ability to self-assemble in aqueous solution forming core-shell structures[7-9]. The core is formed by the hydrophobic segments, whereas the hydrophilic segments form the shell which provides solubility in water and stability to the aggregates. A number of hydrophilic polymers have been used but poly(ethylene glycol) PEO is the most common due to its unique properties, and many studies on PEO-based copolymers have been reported[10-12]. Recently, poly(2-hydroxyethyl methacrylate) (PHEMA)) has attracted great interest because this polymer exhibits excellent biocompatibility[13] and good blood compatibility[14]. PHEMA is a commercially available polymer and find a number of interesting applications, such as hydrogels[15,16], soft contact lenses applications[17], tissue engineering[18]. These features have prompted much interest on block copolymers containing PHEMA[19-21]. Since the discovery of atom transfer radical polymerization (ATRP)[22,23] a number of polymers has been synthesized by using this technique[24]. In particular, homopolymers of HEMA and HEMA-based block copolymers of controlled molecular weight and low polydispersity have been synthesized by ATRP[20,25-31]. Due to poor solubility of PHEMA in non polar solvents ATRP has been carried out in methanol[28] and a combination of methyl ethyl ketone and 1-propanol (70:30 v/v)[25], but high molecular weights could not be obtained. To overcome these difficulties an alternative approach that involves three steps has been used: protection of the hydroxyl group of HEMA, ATRP polymerization of the less polar monomer, and subsequent removal of the protecting groups[31,32].

The aim of this work is to investigate the thermal properties in bulk, and self-assembling in aqueous solution, of amphiphilic block copolymers formed by PMMA and PHEMA as a function of the polymer structure.

2. EXPERIMENTAL PART

2.1 Materials. Tetrahydrofurane (THF, Aldrich), dichloromethane (Aldrich), imidazole (Merck), p-Toluenesulfonyl chloride (TosCl, Merck), *tert*-butyldimethylchlorosilane (TBDMS, Merck), 2,2`-bipyridine (bpy, Aldrich) and tetrabutylammonium fluoride ($(C_4H_9)_4NF$, 1.0 M solution in THF Aldrich) were used without further purification. N,N,N´,N´´,N´´-pentamethyldiethylenetriamine (PMDETA, 98% Aldrich) was purified by passing through a neutral alumina column before use. Methyl methacrylate (MMA, Fluka AG) was washed three times with 5% aqueous NaOH solution and once with distilled water to remove any inhibitor. The solution was dried over $MgSO_4$, filtered, and then distilled under reduced pressure from CaH_2.

2.2 Purification of catalyst. Copper (I) chloride (Merck) was purified by reducing Cu(II) with sodium sulfite according to the following procedure: An aqueous solution of sodium sulfite is added slowly, with constant stirring, to a CuCl solution. Solid CuCl is obtained by adding an excess of sulfurous acid solution. The precipitate is washed with glacial acetic acid and ethanol and dried under vacuum for 8 h. 2-hydroxyethyl methacrylate (HEMA, Aldrich 85%) was distilled under reduced pressure using a Glass Oven B-585 Kugelrohr (Buchi) and then passed through a neutral alumina column.

2.3 Synthesis of HEMA-TBDMS. The protected monomer HEMA-TBDMS was synthesized following a reported method for anionic polymerization[33]. HEMA (5.37 g, 0.041 mol) in THF (50 mL) and imidazole (5.6 g, 0.082 mol) in THF (50 mL) were mixed into a three-neck-flask equipped with thermometer, condenser, and nitrogen bubbling. After cooling to 0 ºC TBDMS (6.20g, 0.041 mol) in CH_2Cl_2 (30 mL) was added slowly under stirring. After 18 h the white salt precipitate was filtered, the residue was redissolved in THF and passed through a neutral alumina column. The solvent was eliminated under reduced pressure and the product was dried at 50 C for 24 h. IR: ν (cm^{-1}) 2957, 2927, 2854 (m, $(CH)_3$), 1718 (s, C=O), 1170, 1110 (C-O-CH_2), 1637 (s, C=C), 941 (s, O-Si-CH_3), 1250 and 836 (s, $Si(CH_3)_3$)

2.4 Synthesis of macroinitiator. The macroinitiators, PMMA-Cl, were obtained by ATRP using CuCl/PMDETA as catalyst. In a typical polymerization experiment, PMDETA (36.4 mg, 0.21 mmol), CuCl, (10.4 mg, 0.105 mmol) and MMA (4.68 g, 46.7 mmol) are mixed in a Schlenk flask. Oxygen is removed by three cycles of freeze–vacuum–thaw ($1.33x10^{-4}$ kPa). Then, p-TosCl (40 mg, 0.209mmol) in 5 mL of THF is added under nitrogen atmosphere, and the mixture was heated at 90ºC for 8 hours with magnetic stirring. After this time, the solution was exposed to air and diluted with THF. The solution was passed through a neutral alumina column to remove the copper catalyst. The resulting solution was precipitated twice by pouring it on methanol, and then dried at 30°C under vacuum to a constant weight. Yield: 96%. ^{1}H NMR (acetone-d_6), 400 MHz: δ 8.0–7.5 (d, ArH), 3.5–3.8 (s, OCH_3), 2.5 (s, CH_3-Ar), 2.0–1.7 (m, CH_2), 1.02–0.83 (s, CH_3)

2.5 Synthesis of PMMA-b-PHEMA. This block copolymer was synthesized in two steps: ATRP polymerization of protected HEMA using PMMA-Cl as macroinitiator, followed by the deprotection reaction. In a typical experiment, the macroinitiator PMMA-Cl (473 mg, 0.0172 mmol M_n =2.75 $x10^4$) was dissolved in 3 mL of a 30:70 mixture of propanol and butanone. The solution is degassed by N_2 bubbling during 15 min. In a Schlenk flask, with magnetic stirring, BPy, (0.011g, 0.0704 mmol), CuCl (0.035g, 0.354 mmol), and HEMA-TBDMS (1.07 g, 0.0412 mmol) were mixed. The mixture was degassed by three freeze–vacuum–thaw cycles and a strong red color is observed. After the Schlenk flask was heated at 65 ºC for 5 min, the macroinitiator solution was added. The mixture is reacted by 12 h at 65 ºC. This mixture was dissolved in 5 mL of THF and the corresponding solution was purified by passing it through a silica column to completely remove the catalyst.

To hydrolyze the TBDMS groups in the resulting polymers a solution of $(C_4H_9)_4NF$ in THF (0.028 mL, 0.028 mmol) was added to (PHEMA-TBDMS)-

e-mail: aolea@unab.cl

b-PMMA (0.1 g, 0.002 mmol) dissolved in 5 mL of THF. The solution was stirred at 25 °C for 24 h. The deprotected polymer was precipitated by pouring the solution into methanol/water (90:10). The yield was 95%. IR: ν (cm^{-1}): 3600 (CH_2-OH), 1718 (s, C=O), 1170–1110 (C-O-CH_2). ^{1}H–NMR (acetone-d_6), 400 MHz: δ 8.0, 7.5 (d, ArH), 3.5–3.8 (s, OCH_3), 3.8–4.0 (d, OCO-CH_2-CH_2), 2.5 (s, CH_3-Ar), 2.0–1.7 (m, CH_2), 1.5–1.8 (s, CH_3).

2.6 Copolymer Characterization. The number average (M_n) and weight average (M_w) molecular weights were determined by size exclusion chromatography (SEC) using a LC-20AD Prominence, Shimadzu with RI detector, and two GPC columns (MZ-Gel SD plus 10000 and 100000 A). The data was stored and processed with Class VP software. The samples were dissolved in THF (20 mg/mL) and eluted with THF at a flow rate of 0.400 mL/min. The calibration curve was performed using polystyrene standards**.**

FT–IR spectra were recorded on a Bruker Vector 22 (Bruker Optics GmbH, Inc., Ettlingen, Germany) spectrometer. ^{1}H–NMR spectra were recorded in solution at room temperature with a Bruker Avance 400 Digital (Bruker, Karlsruhe, Germany) spectrometer using deuterated acetone as the solvent.

2.7 Thermal behavior. The thermal stability and glass transition temperatures of the polymers were determined by Thermal Gravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC), respectively.

Thermal stability studies were performed using a TGA Q50, TA Instruments. The instrument was calibrated both for temperature and weight by usual methods. The weight loss percentage was determined over the temperature range 20 to 600 ºC at a scan rate of 10 ºC/min. The average sample weight was 6 mg and the dry nitrogen flow rate 40 mL/min. The glass transition temperatures were determined by using a Mettler Toledo Star System 822e. DSC measurements were carried out to determine the copolymer's glass transition temperature (Tg). The Tg was measured at a heating rate of 10 ºC/min under dry nitrogen (25 mL/min) over a temperature range from 30 to 200 ºC. To eliminate the effect of thermal history on the phase transitions, all samples were heated to 150 °C, held at that temperature for 5 min and then cooled to 30°C.

3. RESULTS AND DISCUSSION

3.1 Synthesis of polymers. The amphiphilic block copolymer PMMA-b-PHEMA was synthesized by two successive ATRP polymerizations. Firstly, well-defined chloride terminated PMMA chains were obtained by ATRP using p-TosCl/CuCl/PMDETA system. A series of PMMA-Cl with different molecular weights was synthesized by varying the initiator concentration. The characterization of PMMA-Cl was carried out by FTIR, ^{1}H-NMR, and SEC. The SEC results presented in Table 1 show that the molecular weight of the formed polymer decreases linearly with increasing p-TosCl concentration. The data of Table 1 show that polymers with a relatively low polydispersity PD, of different degrees of polymerization DP, can be obtained. These results indicate that p-TosCl/PMDETA is an effective initiator system, and confirm that ATRP systems using PMDETA as metal complex ligand afford polymers in high yields and with narrow molecular weight distribution[31].

Table 1. Results of SEC measurements for ATRP polymerization of MMA in THF using p-TosCl/PMDETA as initiator system.

PMMA	p-TosCl (mmol)	Yield	Mn	Mw	PD	DP
H1	0.525	85.2	6700	7360	1.09	67
H2	0.399	92.1	20760	23380	1.13	207
H3	0.266	94.4	27540	36850	1.33	275
H4	0.199	77.4	33020	47650	1.44	330
H5	0.133	92.5	56250	58830	1.05	562

In the second step, hydrophilic blocks of PHEMA were added to PMMA polymer chains by using PMMA-Cl as part of the initiating system in an ATRP polymerization. Thus, the amphiphilic character of the block copolymer can be modulated by using PMMA-Cl of different molecular weight as macroinitiator, and/or by varying the degree of polymerization of HEMA in the second block (see Table 2). The initial attempt to polymerize HEMA with **H3** gave a polymer with a very low number of HEMA units, probably due to poor solubility of PHEMA in organic solvents. For this reason the monomer was polymerized in its protected form, and TBDMS was used as protective group because it exhibits higher stability compared to trimethylsilane. The ATRP conditions were similar to those used to polymerize PMMA, and the degree of polymerization for the PHEMA block was varied by changing the feeding ratio of protected HEMA. The characterization of PMMA-b-PHEMA was carried out by FTIR, ^{1}H-NMR, and SEC. In Figure 1 are compared the SEC chromatograms obtained for the macroinitiator **H2** and the block copolymer **C2**.

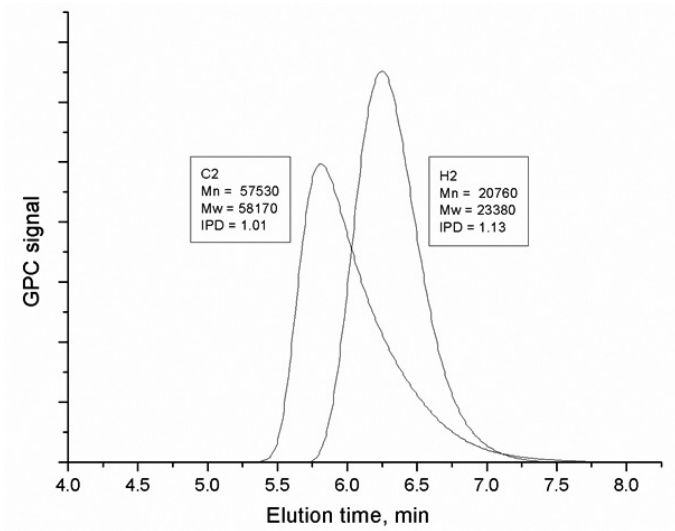

Figure 1. SEC chromatograms of PMMA-Cl (**H2**) and block copolymer PMMA-b-PHEMA protected with TBDMS (**C2**). Both polymers were dissolved in THF.

The molar mass distributions of both polymers are monomodal indicating that no homopolymers of HEMA were formed. The molecular weight and polydispersities of block copolymers are summarized in Table 2.

Table 2. Molecular weights, polydispersities and composition of block copolymers.

Sample	PMMA-Cl	Mn	Mw	PD	Composition
C1	H1	44230	45260	1.02	$PMMA_{67}$-b-$PHEMA_{154}$
C2	H2	58170	57530	1.01	$PMMA_{207}$-b-$PHEMA_{153}$
C3	H2	53690	53210	1.01	$PMMA_{207}$-b-$PHEMA_{135}$
C4	H3	28880	36850	1.27	$PMMA_{275}$-b-$PHEMA_{10}$
C5	H3	49130	52820	1.07	$PMMA_{275}$-b-$PHEMA_{88}$

The results indicate that ATRP polymerization allows chain extension of PMMA and the growth in molecular weight can be attributed exclusively to PHEMA block formation. The different degrees of polymerization of this block and the low values of polydispersities indicate that a good control of block copolymerization is achieved by using PMMA-Cl as macroinitiator.

Finally, the block copolymers were reacted with $(C_4H_9)_4NF$ in order to remove the TBDMS groups that were used to protect the hydroxyl groups. The complete removal of the TBDMS and formation of hydroxyl groups was confirmed by FTIR and ^{1}H–NMR.

Recently, a different approach to synthesize amphiphilic block copolymers containing a higher ratio of HEMA has been reported[29]. In this scheme PHEMA-Cl is used as macroinitiator, and block copolymers of PHEMA with PS and poly(phenylmaleimide) were obtained without group protection[29].

3.2 Thermal Analysis. The thermal behavior of PMMA-Cl and PMMA-b-PHEMA was investigated by TGA and DSC. The TGA curves obtained for the different PMMA macroinitiators and block copolymers are shown in Figures 2 and 3, respectively.

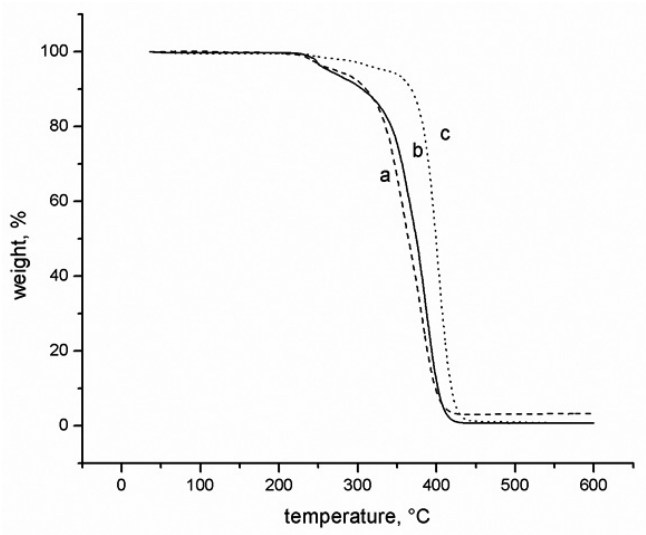

Figure 2. TGA thermograms of PMMA-Cl of different degrees of polymerization: (a) H1; (b) H2; (c) H3.

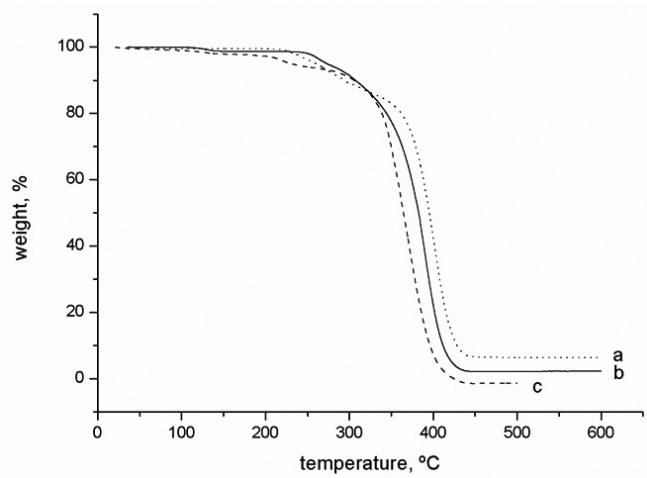

Figure 3. TGA thermograms of PMMA-b-PHEMA of different composition: (a) C1; (b) C2; (c) C4.

From the TGA curves the temperatures of 5% and 50% mass loss, $T_{5\%}$, $T_{50\%}$, were obtained. In addition, from the derivative of weight loss curves the temperatures of maximum loss were determined. The results are summarized in Table 3. The derivatives of TGA curves show a single peak, which indicate one reaction stage for thermal degradation. For all studied systems the main part of mass loss occurs above 350 ºC, suggesting that degradation is due to random chain scission[34]. On the other hand, the TGA curves obtained for some PMMA-b-PHEMA block copolymers exhibit initial degradation at lower temperatures, which can be attributed to water linked to the hygroscopic PHEMA block. In HEMA polymers and copolymers bound water might reach up to 10% of the mass loss[29,35].

The glass transition temperatures of PMMA-Cl and block copolymers were determined by DSC. For all block copolymers and PMMA homopolymers, a single glass transition temperature is detected, and their values depend slightly on copolymer composition and on molecular weight of PMMA (see Figures 3-4). This suggests that the copolymers have a random copolymer structure for all compositions. However, for all block copolymers the T_g values obtained are lower than those measured for the respective PMMA-Cl, and higher than the T_g of pure PHEMA (87 ºC)[35]. These results indicate that in the glassy state the polymer chains are statistically distributed, and no microphase structures are formed by the amphiphilic block copolymer.

Table 3. Glass transition temperature T_g, temperatures of 5% and 50% mass loss $T_{5\%}$, $T_{50\%}$, and maximum temperature of mass loss T_{max}.

Polymer	T_g (ºC)	$T_{5\%}$ (°C)	$T_{50\%}$ (°C)	T_{max} (°C)	% mass loss
$PMMA_{67}$	116.3	335	399	399	48.7
$PMMA_{207}$	121.7	263	374	387	70.0
$PMMA_{275}$	122.9	272	364	384	74.8
$PMMA_{67}$-b-$PHEMA_{154}$	108.8	260	395	402	61.4
$PMMA_{207}$-b-$PHEMA_{135}$	-	136	372	388	74.7
$PMMA_{207}$-b-$PHEMA_{153}$	116.0	273	383	391	63.7
$PMMA_{275}$-b-$PHEMA_{88}$	113.9	176	371	376	56.4

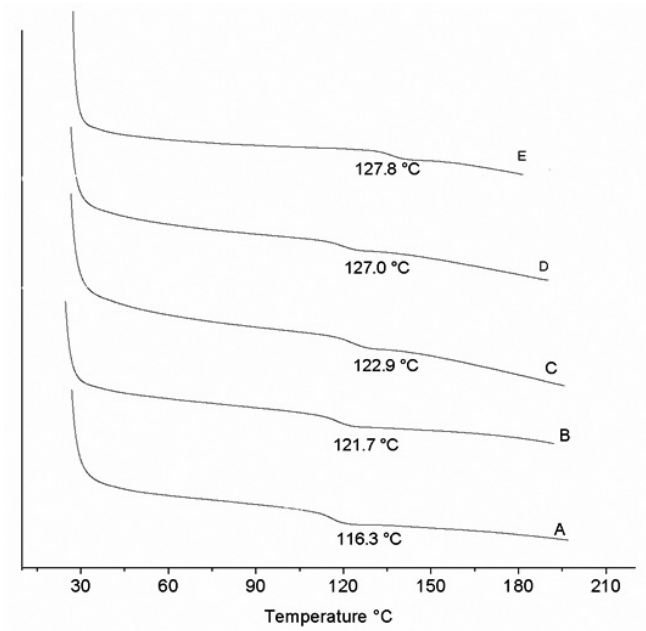

Figure 4. DSC thermograms of macroinitiators PMMA-Cl: (A) H1; (B) H2; (C) H3; (D) H4; (E) H5.

3.3 Self-assembly of diblock copolymers in aqueous solution. The self-assembly of PMMA-b-PHEMA in aqueous solution was monitored by fluorescence probing methods and using pyrene as fluorescent probe. Pyrene has been widely used in the study of microheterogeneous systems because its fluorescence and excitation spectra changes with the polarity of the environment where it is located[36]. Based on the changes of emission and excitation spectra of pyrene with polymer concentration several methods to determine the critical micelle concentration CMC of block copolymers have been proposed[37,38]. The most accepted method has been proposed by Wilhelm et al. and uses the effect of polymer concentration on the excitation spectra of pyrene[38]. Briefly, the excitation spectra exhibit a red shift of the band (0,0) from 333 to 338 nm upon the increment of block copolymer concentration (see figure 6). The extreme values of the ratio I_{338}/I_{333} = F allow the measurement of the ratio of pyrene solubilized into the micelle over the concentration of pyrene in the aqueous phase according to

$$\frac{[Py]_M}{[Py]_W} = \frac{F - F_{\min}}{F_{\max} - F} = KC \qquad (1)$$

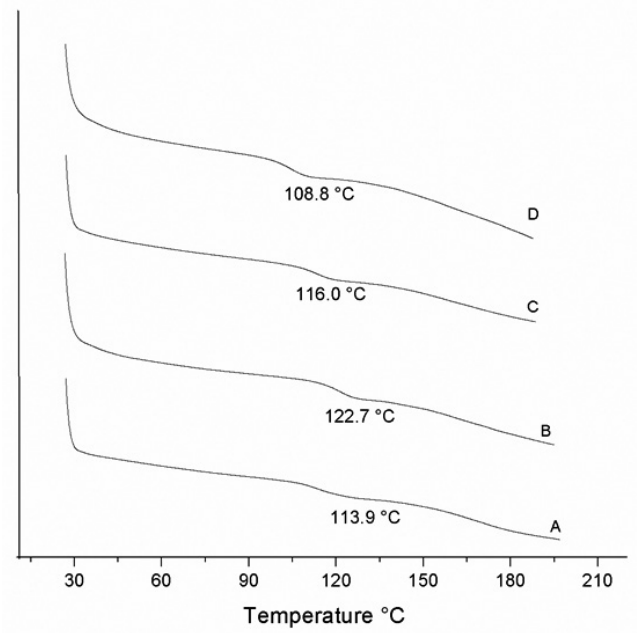

Figure 5. DSC thermograms of block copolymers: (A) C5; (B) C4; (C) C2; (D) C1.

where K is a constant that includes the distribution constant of pyrene between the aqueous and micellar phases, and C represents the polymer concentration. In a plot of this ratio against polymer concentration the data can be fitted to two intersecting straight lines, and the CMC is given by the extrapolated intercept with the C axis. In figure 7 are shown the results obtained by plotting Wilhelm's equation for C4 block copolymer. The CMC values obtained with this method are in the range 10^{-6} – 10^{-7} M (see table 4), and they are similar to those reported for block copolymers based on polystyrene PS[5,6,37,38].

The data indicate that the CMC depends on the size of the hydrophilic block, i.e. for copolymers with the same PMMA block, CMC increases with increasing number of HEMA units. In other words, the aggregation starts at lower concentrations in those copolymers with the smallest hydrophilic block. This result suggests that, in addition to the hydrophobic effect of the PMMA chains, the interaction of HEMA groups with water makes an important contribution to the driving force for the aggregation process.

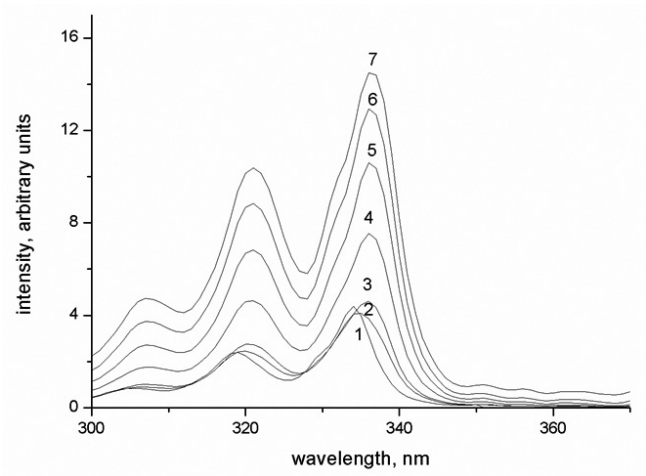

Figure 6. Excitation spectra of pyrene at different concentrations of C4: (1) 0 μM; (2) 29 μM; (3) 57 μM; (4) 140 μM; (5) 350 μM; (6) 890 μM; (7) 2200 μM

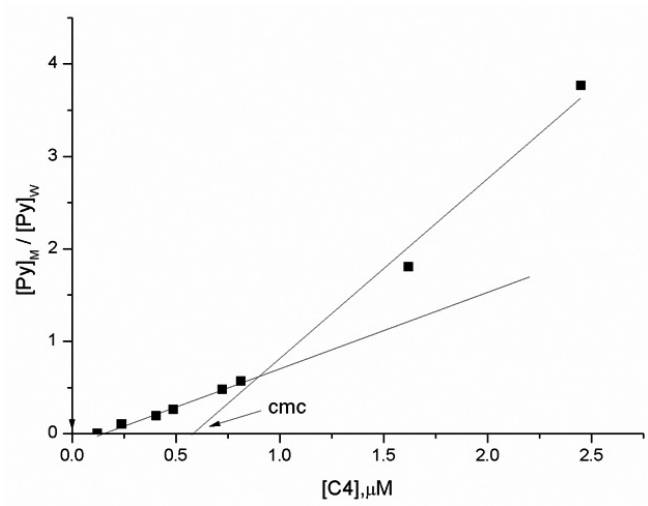

Figure 7. Plot of the ratio $[Py]_M$ / $[Py]_W$ against C4 concentration, according to Wilhelm`s equation (Ref. 37).

Table 4. Critical micelle concentration CMC and ratio I_1 / I_3 of block copolymers.

Block copolymer	PMMA-Cl	Composition	CMC (M)	I_1 / I_3
C1	H1	$PMMA_{67}$-b-$PHEMA_{154}$	$9.0x10^{-7}$	1.33
C2	H2	$PMMA_{207}$-b-$PHEMA_{153}$	$8.2x10^{-7}$	1.42
C3	H2	$PMMA_{207}$-b-$PHEMA_{135}$	$6.9x10^{-7}$	1.45
C4	H3	$PMMA_{275}$-b-$PHEMA_{10}$	$1.0x10^{-7}$	1.37
C5	H3	$PMMA_{275}$-b-$PHEMA_{88}$	$5.8x10^{-7}$	1.46

The ratio I_1/I_3 of the intensities of the bands that appear at 380 nm (I_1) and 390 nm (I_3) has been proposed as an empirical polarity scale[36,39]. At high polymer concentration (above CMC) the value of the ratio I_1/I_3 represents the polarity sensed by pyrene in the hydrophobic sites provided by the polymer micelle. Therefore, a comparison of these values provides a relative measure of the micelle micropolarity. The data in table 4 show that the values of the ratio I_1/I_3 vary slightly with the copolymer composition, i.e. 1.33 – 1.46. This result suggests that increasing the number of MMA units from 67 to 275, or the number of HEMA units from 10 to 154, has not effect on the core hydrophobicity. On the other hand, the micropolarity sensed by pyrene in these micelles is higher than that determined in aggregates formed by block copolymers where PS is the hydrophobic block[5,6,38].

4. CONCLUSIONS

In this study amphiphilic block copolymers of PMMA and PHEMA with different block lengths have been synthesized by two successive ATRP polymerizations. The results indicate that a good control of copolymerization is achieved by using chloride terminated PMMA as macroinitiator. The amphiphilic character of the block copolymer was modulated by varying the molecular weight of PMMA-Cl, and/or by varying the degree of polymerization of HEMA in the second block. Thermal degradation studies of both PMMA and block copolymers PMMA-b-PHEMA indicate that degradation occurs in one stage and is due to random chain scission. In addition, single glass transition temperatures were detected for all polymers indicating that in the glassy state the polymer chains are statistically distributed.

The self-assembly of PMMA-b-PHEMA in aqueous solution was investigated by fluorescence probing. Interestingly, the critical micelle concentration depends both on the relative sizes of hydrophobic and hydrophilic blocks. This result suggests that the free energy of micellization receives contributions from the hydrophobic effect and from the interaction between water and the polar block.

ACKNOWLEDGMENTS

This work has been funded by UNAB DI-309-13/R and FONDECYT No 1130742. B. Acevedo thanks UNAB for Ph.D. fellowship.

REFERENCES

1. M. L. Adams, A. Lavasanifar, and G. S. Kwon *J. Pharm. Sci.*, 92, 1343 (2003)
2. K. Kataoka, A. Harada, and Y. Nagasaki *Adv. Drug Deliv. Rev.*, 47, 113 (2001)
3. A. V. Kabanov and V. Y. Alakhov, in *Amphiphilic Block Copolymers. Self-assembly and applications*, P. Alexandridis and B. Lindman, Ed., Elsevier. Amsterdam, 2000.
4. C. Allen, D. Maysinger, and A. Eisenberg *Colloids Surf. , B*, 16, 3 (1999)
5. B. Urbano, P. Silva, A. F. Olea, I. Fuentes, and F. Martinez *J. Chil. Chem. Soc.*, 53, 1507 (2008)
6. A. F. Olea, P. Silva, I. Fuentes, F. Martinez, and D. Worrall *J. Photochem. Photobiol. A: Chem.*, 217, 49 (2011)
7. Z. S. Gao and A. Eisenberg *Macromolecules*, 26, 7353 (1993)
8. G. H. Zhang, K. Khougaz, M. Moffitt, and A. Eisenberg, in *Amphiphilic Block Copolymers. Self-assembly and applications*, P. Alexandridis and B. Lindman, Ed., Elsevier. Amsterdam, 2000.
9. P. Alexandridis and Lindman B., *Amphiphilic Block Copolymers, Self-Assembly and Applications*, Elsevier Science, Amsterdam, 2000
10. R. L. Xu, M. A. Winnik, G. Riess, B. Chu, and M. D. Croucher *Macromolecules*, 25, 644 (1992)
11. K. Yu and A. Eisenberg *Macromolecules*, 31, 3509 (1998)
12. P. Alexandridis and T. A. Hatton *Colloids Surf. , A*, 96, 1 (1995)
13. I. Volfova, B. Rihova, V. Vetvicka, P. Rossman, and K. Ulbrich *J. Bioact. Compat. Pol.*, 7, 175 (1992)
14. M. Fischer, C. P. Baptista, I. C. Goncalves, B. D. Ratner, C. Sperling, C. Werner, C. L. Martins, and M. A. Barbosa *Biomaterials*, 33, 7677 (2012)
15. B. D. Ratner and A. S. Hoffman, in *Hydrogels for Medical and Related Applications*, J. D. Andrade, Ed., ACS Symposium Series, American Chemical Society. Washington, 1976.
16. F. Chiellini, F. Petrucci, E. Ranucci, and R. Solaro *J. Appl. Polym. Sci.*, 85, 2729 (2002)
17. P. C. Nicolson and J. Vogt *Biomaterials*, 22, 3273 (2001)
18. S. Atzet, S. Curtin, P. Trinh, S. Bryant, and B. Ratner *Biomacromolecules*, 9, 3370 (2008)
19. L. Yuan, W. L. Chen, J. Li, J. H. Hu, J. J. Yan, and D. Yang *J. Polym. Sci. Part A-Polym. Chem.*, 50, 4579 (2012)
20. F. J. Xu, H. Z. Li, J. Li, Z. X. Zhang, E. T. Kang, and K. G. Neoh *Biomaterials*, 29, 3023 (2008)
21. K. Ishizu, S. Takano, T. Murakami, S. Uchida, and M. Ozawa *J. Appl. Polym. Sci.*, 109, 3554 (2008)
22. M. Kato, M. Kamigaito, M. Sawamoto, and T. Higashimura *Macromolecules*, 28, 1721 (1995)
23. J. Wang and K. Matyjaszewski *J. Am. Chem. Soc.*, 117, 5614 (1995)
24. K. Matyjaszewski and J. Xia *Chem. Rev.*, 101, 2921 (2001)
25. K. L. Beers, S. Boo, S. G. Gaynor, and K. Matyjaszewski *Macromolecules*, 32, 5772 (1999)
26. K. L. Robinson, M. A. Khan, M. V. D. Banez, X. S. Wang, and S. P. Armes *Macromolecules*, 34, 3155 (2001)
27. T. L. Wang, Y. Z. Liu, B. C. Jeng, and Y. C. Cai *J. Polym. Res.*, 12, 67 (2005)
28. J. V. M. Weaver, I. Bannister, K. L. Robinson, X. Bories-Azeau, S. P. Armes, M. Smallridge, and P. McKenna *Macromolecules*, 37, 2395 (2004)
29. G. D. Pizarro, O. G. Marambio, M. Jeria-Orell, M. E. Flores, and B. L. Rivas *J. Appl. Polym. Sci.*, 118, 3649 (2010)
30. R. P. Johnson, Y. I. Jeong, E. Choi, C. W. Chung, D. H. Kang, S. O. Oh, H. Suh, and I. Kim *Adv. Funct. Mater.*, 22, 1058 (2012)
31. M. Yin, W. A. Habicher, and B. Voit *Polymer*, 46, 3215 (2005)
32. K. L. Beers, S. G. Gaynor, K. Matyjaszewski, S. S. Sheiko, and M. Moller *Macromolecules*, 31, 9413 (1998)
33. H. Mori, O. Wakisaka, A. Hirao, and S. Nakahama *Macromol. Chem. Physics*, 195, 3213 (1994)
34. J. L. de la Fuente, M. Wilhelm, H. W. Spiess, E. L. Madruga, M. Fernandez-Garcia, and M. L. Cerrada *Polymer*, 46, 4544 (2005)
35. T. Caykara, C. Ozyurek, and O. Kantoglu *J. Appl. Polym. Sci.*, 103, 1602 (2007)
36. K. Kalyanasundaram and J. K. Thomas *J. Am. Chem. Soc.*, 99, 2039 (1977)
37. I. V. Astafieva, X. F. Zhong, and A. Eisenberg *Macromolecules*, 26, 7339 (1993)
38. M. Wilhelm, C. L. Zhao, Y. C. Wang, R. L. Xu, M. A. Winnik, J. L. Mura, G. Riess, and M. D. Croucher *Macromolecules*, 24, 1033 (1991)
39. D. C. Dong and M. A. Winnik *Photochem. Photobiol.*, 35, 17 (1982)